the applicants' claims also distinguish patentably over the references applied by the Examiner in paragraphs 4 and 5 of the Action.

More specifically, the Examiner is requested to reconsider the Section 103 rejections of claims 1, 3-17, 21-27, 29 and 31-41 as unpatentable over the newly cited Murrer et al patent (5,021,409). The reference does not suggest the applicants' invention or make it obvious.

In rejecting the applicants' claims, the Examiner states that Murrer et al teaches a generic group of compounds which embraces the applicants' compounds. However, with respect, the applicants submit that the Examiner's view of Murrer et al. is not correct. Thus, the compounds of the present application have two cyclic moieties which are linked by a methylene-aromatic/heteroaromatic-methylene group. compounds disclosed in Murrer have two cyclic moieties which are linked by amongst other things alkylene, aryl or fused aryl. Up to six of the selected group A may be linked together, but the general formula of Murrer does <u>not</u> say "wherein A is selected from one or more of ...". Thus, a compound where the two cyclic moieties are linked by methylene-aromatic/heteroaromatic-methylene is not delivered or contemplated by, or within the scope of, Murrer et al. present application does not therefore recite specific species and/or a more limited subgenus of the reference. Furthermore,

there is no teaching in the reference that would lead a skilled man to the compounds of the present invention.

In view of the foregoing, the applicants respectfully submit that the Section 103 rejection based on Murrer et al. should be withdrawn. This is true for all of the applicants' claims although it is further noted that there is nothing in Murrer et al. that can be said to be suggestive of the compounds called for in the applicants' dependent claims, e.g., claims 4-17, 21-27, 29 and 31-41. Nothing in Murrer et al. would suggest to one in the art the specific compounds called for in these claims. The Examiner will know that structural modifications can have marked and unpredictable effects on the properties of compounds. The structural differences between the reference products and the applicants' compounds are significant and cannot be dismissed as obvious, bearing in mind especially the unpredictability of the effects of structural changes in compounds of the present type.

The Examiner is also requested to reconsider the Section 103 rejection of claims 6-17, 25-27, 29 and 31-41 as unpatentable over Murrer et al. in view of WO 92/16494. The Examiner's combination of references is not in any sense warranted since there is no motivation in either reference to make the modifications in the Murrer compounds which are necessary to reach the applicants' compounds.

As earlier noted, Murrer et al. disclose a compound having two cyclic moieties linked by amongst other things

alkylene, aryl or fused aryl. WO 92/16494 discloses compounds having a polyheterocyclic moiety and a polyheteroalkyl chain, these two groups being linked by amongst other things aryl and alkylarylalkyl. Claims 11-15, 29-35 and 41 of the present application call for compounds having two polyheterocyclic moieties linked by methylene-heteroaromatic-methylene. Since neither Murrer nor WO '494 discloses compounds wherein the linking group A is methylene-heteroaromatic-methylene, the two references (even if considered together when there is really no reason in the art to do so), would not have motivated one of ordinary skill in the art to prepare the applicants' compounds. In brief, therefore, the references do not make the applicants' invention obvious, there being no motivation in the references to make the changes needed to reach the applicants' invention.

The foregoing comments should be fully dispositive of the Examiner's art rejections against all of the claims. However, it is also noted that claims 8 and 29 require that the applicants' linking group is <a href="mailto:methylene-biphenyl-methylene">methylene</a>. Such a group is not disclosed in either of the Examiner's two references. This is a further basis for finding claims 8 and 29 allowable over the reference disclosures.

It is also noted that claim 38 discloses compound with a linking group methylene-phenyl-methylene wherein the phenyl is substituted by two methyl groups. Such a linking group is not specifically disclosed in WO '494. Although linking groups of

the type alkyl-phenyl-alkyl wherein the phenyl moiety is substituted are disclosed, the substituents chosen are very specific and thus a skilled person would be led to believe that these were the only substituents that gave activity and there would be no motivation to try others. This is another reason why claim 38, for example, should be viewed as allowable over the art.

It is also noted that while claims 6, 7, 9, 10, 16, 17, 25, 26, 27, 36, 37, 39 and 40 all have a linking group which is within the scope of linking group A of WO '494, the reference does not disclose any specific examples of this linking group. Furthermore, the activities of the compounds of the present invention are at least 100 times that of the compound tested in WO '494 and the selectivity index is also considerably improved. Such an improvement in activity and selectivity could not have been predicted by a skilled person when combining the teachings of the two cited references. For these reasons as well, the indicated claims should be considered allowable over the art.

The Examiner's comments regarding applicants' priority benefit for claims 6-17, 25-27, 29 and 31-41 have been noted. The applicants do not agree with the Examiner's position. However, the point is deemed to be moot in view of the foregoing comments in favor of the nonobvious nature of the applicants' invention and the allowability of the claims herein.

Favorable reconsideration is requested.

Respectfully submitted,

CUSHMAN DARBY & CUSHMAN, L.L.P.

Paul N. Kokulis Reg. No. 16773

PNK:lal

1100 New York Avenue, N.W.

Ninth Floor Washington, D.C. 20005-3918

Phone: (202) 861-3503